effected in regard to the pathology of phosphate of lime; but now that the frequency of its occurrence in human urine as a crystallized deposit is made known, its pathology, apart from that of the triple phosphate, will no doubt be specially considered.

It will be apparent from the following quotation, that the late Dr. Golding Bird regarded deposits of phosphate of lime as of more consequence than those of the triple phosphate:—"The pathological state of the system accompanying the appearance of deposits of phosphate of lime is analogous to that occurring with the triple phosphate; indeed, as has been already observed, they often, and in alkaline urine always, occur simultaneously. So far as my own experience has extended, when the deposit has consisted chiefly of the calcareous salt, the patients have appeared to present more marked evidence of exhaustion, and of the previous existence of some drain on the nervous system, than when the triple salt alone existed, unless its source is strictly local."

It should be remembered that these remarks of Dr. Bird refer to deposits of phosphate of lime in *the granular state*, and not to the crystalline deposits, with the occurrence of which he was unacquainted. I have already stated that, according to my experience, the granular calcareous phosphatic deposits are much more rare than the crystalline.

It follows from these observations and investigations:—

First. That deposits of *crystallized* phosphate of lime are of frequent occurrence in human urine, much more so, indeed, than those of the amorphous or granular form of that phosphate.

Second. That the crystals present well-marked and highly characteristic forms, whereby the identification of this phosphate by means of the microscope is rendered easy and certain.

Third. That there is good reason to believe that deposits of phosphate of lime are of greater pathological importance than those of the phosphate of ammonia and magnesia.

February 2, 1860.

Sir BENJAMIN C. BRODIE, Bart., President, in the Chair.

In accordance with notice given at the last meeting, the Right Honourable Sir Edward Ryan, Member of Her Majesty's Privy Council,

was proposed for election and immediate ballot; and the ballot having been taken, Sir Edward Ryan was declared duly elected.

The following communications were read:—

I. "On the Saccharine Function of the Liver." By GEORGE HARLEY, M.D., F.C.S., Professor of Medical Jurisprudence in University College, London. Communicated by Dr. SHARPEY, Sec. R.S. Received December 19, 1859.

Although it is nearly 200 years since our countryman, the celebrated Dr. Thomas Willis, made the important discovery of the occasional presence of sugar in the human urine, it was not, until very recently, known that the formation of saccharine matter is constantly going on in the healthy animal body.

Since Bernard, in 1848, communicated to the French Academy the discovery of the saccharine function of the animal organism, physiologists in all countries have more or less directed to it their attention. For a time various opinions were held by different observers regarding the origin of the sugar found in the body; but at length it was generally admitted that the liver had the power of forming a substance to which Bernard gave the name *Glucogen*; that this peculiar substance was transformed into sugar; and that the sugar in its turn disappeared in the capillaries of the different organs and tissues of the body.

In the summer of 1858, however, Dr. Pavy read a paper on the "Alleged Sugar-forming Function of the Liver" before the Royal Society, the object of which was to prove that the presence of sugar in the animal economy is "due to a *post mortem* occurrence,"—that as long as life continues, glucogen only is to be found, and not until after death does the transformation of this substance into sugar begin.

The question of the saccharine function of the liver being a subject to which I have more or less directed my attention since 1853, when I communicated to the Société de Biologie de Paris an account of an experimental procedure whereby diabetes can be produced artificially in animals, the above-mentioned paper was to me one of peculiar interest. The conclusions of the author were so much opposed to the results of my own experiments, as well as those of other observers, that I felt anxious to test them.

Accordingly, having received the kind offer of Professor Sharpey's cooperation, I undertook a series of experiments, the results of which I beg the honour of communicating to the Royal Society.

As the experiments performed were merely a repetition of some of those made by previous inquirers, I shall not enter into detail further than is necessary to explain the precautions adopted with the view to avoid error. And, looking at the object in view, it will readily be understood why in the present instance the tests employed for the detection of the sugar were limited to caustic potash with and without sulphate of copper. The mode of proceeding was as follows:—In testing the blood, a quantity of distilled water, equal to about four times that of the blood used, was boiled in a capsule. To the water, when boiling, were added a few drops of acetic acid, and afterwards the blood was very gradually introduced. In order that the albumen might be thoroughly coagulated, a drop or two more of acetic acid was added, care being taken to avoid an excess. When the albumen was completely coagulated, which was known by its separating and floating in the clear liquid, the whole was thrown on a filter. The clear filtered liquid was then tested. The same process was followed when operating on the liver.

The first point to be ascertained was whether, under favourable circumstances as regarded diet, sugar could be found in the circulation. The following experiment proved this.

Exp. 1. From the carotid artery of a rough terrier dog, three hours after being fed on bread, milk, and boiled liver, a portion of blood equal to about three-fourths of an ounce was withdrawn. This, on being treated in the manner explained, gave distinct evidence of the presence of sugar. A second portion of blood, after standing thirty-five minutes in a room of moderate temperature, yielded a similar result.

As in this instance a few seconds elapsed between the withdrawal of the first portion of blood and its treatment with the boiling acidulated water, and as it was possible that in these few seconds the sugar might have been formed from the glucogen present in the circulation, we (Professor Sharpey and myself) thought it advisable in our next experiment to allow the blood to flow directly from the artery into the boiling mixture, and thereby avoid the possibility of sugar being produced by the transformation of glucogen after the removal of the blood

from the body. It was further desired to operate on an animal in what might be considered its natural condition as to food. Accordingly one that had been running at large was selected, and the following experiment performed:—

Exp. 2. Into the left carotid artery of a small cocker dog was inserted a canula with a stopcock. The animal was then placed so as to allow the blood to flow directly into the boiling acidulated water. The clear filtered liquid from this blood became of a yellow tint on being boiled with soda, and gave a red precipitate with the sulphate of copper and potash, thereby indicating the presence of sugar. Two ounces of blood from the same animal were similarly tested after the blood had stood twenty-four hours in a room of moderate temperature, and the result obtained was the same as with the first portion.

The next experiment was made on an animal under conditions, as regards food, unfavourable for the production of sugar. In order, too, to avoid any chance of injuring the sympathetic nerve during the operation, and thereby favouring the formation of sugar in the body, the blood was withdrawn from the right femoral artery instead of the carotid. The following are the particulars of the experiment:—

Exp. 3. A good-sized dog was fed solely on flesh during four days. Three hours after the last meal, which consisted of half a pound of boiled horseflesh, $1\frac{1}{2}$ oz. of blood was permitted to flow from the femoral artery directly into the boiling mixture. The solution obtained from this blood, as in the other cases, contained sugar. Another portion of blood, after standing three hours, was tested in the same way, and, as far as could be judged by the eye, contained a similar proportion of sugar.

In neither of the preceding cases was the amount of sugar in the blood quantitatively determined, as I had already done so on many previous occasions; and I knew that in healthy arterial blood it varied according to the state of the digestion, and the kind of food, from an inappreciable quantity up to 0·24 per cent.*

Having been now satisfied that sugar is to be found in the blood of healthy animals at the very moment of its withdrawal from the

* "On the Physiology of Saccharine Urine," by Geo. Harley, M.D., British and Foreign Med. Chir. Rev. July 1857, p. 191–204.

circulation, even when none has been introduced along with the food, we next proceeded to test the grounds upon which it had been asserted that glucogen is not transformed into sugar in the healthy liver during life.

In the paper already referred to, Dr. Pavy stated that the sudden abstraction of heat from the liver after its removal from the body, checks the transformation of the sugar-forming material, and thereby enables us to operate on the hepatic substance while in the same chemical condition as during life. The plan he recommends is to sacrifice a dog by pithing, and instantly to slice off a piece of liver, and throw it into a freezing mixture of ice and salt. In which case he says the absence of sugar is almost complete, and thence concludes that the presence of sugar in the liver can no longer be looked upon as a "natural *ante mortem* condition;" but "is in reality due to a *post mortem* occurrence."

In the following experiments, not only was the plan recommended most scrupulously followed, but even the risk of the glucogen in the liver becoming transformed into sugar during the process of preparing the decoction, was avoided by cutting the frozen liver into thin slices, and allowing them, while still in that condition, to fall directly into the boiling mixture of acetic acid and water. The liver was in this way prevented from thawing until it entered a medium as capable of arresting the transformation of its glucogen into sugar as the cold. The decoction so obtained might therefore be presumed to contain the soluble matters as nearly as possible in the same chemical state as they were in the living organ.

Exp. 4. A small, but full-grown dog was fed during fourteen days solely on animal food. Four hours after a meal of boiled horseflesh he was killed by section of the medulla oblongata. The abdomen was rapidly opened, and a portion of liver cut off and instantly immersed in a freezing mixture of ice and salt. A second portion of liver was as speedily as possible detached, and quickly washed in cold water. The latter portion was then, without loss of time, cut into fragments, which were allowed to fall directly into boiling acidulated water. On testing the clear filtrate, distinct evidence of the presence of sugar was obtained. After half an hour, the frozen portion of liver was taken, without being allowed to thaw, and sliced directly into the boiling water with acetic acid. The

clear liquid yielded in this case as distinct evidence of sugar as in the other. Forty minutes after the death of the animal, another portion of liver, which till then had remained undisturbed in the abdomen, was treated like the others. This gave evidence of containing a much greater quantity of sugar, thus confirming Bernard's statement, that the transformation of glucogen goes on in the liver after its removal from the body, or after the death of the animal.

In order to be perfectly certain that the sugar found in the liver at the instant of its removal from the body was really formed where it was found, and not carried there by the portal blood from the food, the following experiment was performed:—

Exp. 5. A dog was fed during ten days on boiled tripe. Twenty-two hours after the last meal the animal was pithed. In less than twenty seconds a portion of the liver was in the freezing mixture of ice and salt. While I boiled directly another portion of liver, Professor Sharpey put a ligature on the portal vein, and collected its blood. He likewise collected some of the hepatic blood which flowed from the cut liver.

In the portal blood not a trace of sugar could be detected. The hepatic blood, on the other hand, gave distinct evidence of its presence. Both bloods were tested exactly alike. The clear liquids obtained from the frozen liver and from the portion treated directly, notwithstanding that they were filtered while hot, and also tested while still hot, both gave distinct evidence of sugar. On the following day a second portion of portal blood, which had been purposely kept all night in order to ascertain if, on standing some time, sugar would form in it, still yielded the same negative result. Even after treating it with saliva, which would have transformed its glucogen into sugar, had it contained any, no evidence of the presence of sugar was obtained. On the other hand, when saliva was added to the decoctions of the liver above spoken of, a great increase in the amount of sugar was observed. The quantity of sugar so obtained did not appear to be so great, however, as that yielded by a portion of the liver which remained all night untouched in the abdomen of the animal.

Professor Garrod, F.R.S., who was present, not at the commencement of the experiment, but on the following day, when the different decoctions were tested, agreed with Professor Sharpey and myself,

that this experiment showed the truth of Bernard's statement, that the liver might contain both sugar and glucogen when the portal blood contained neither.

The stomach and intestines of this animal were found void of food; the large intestine only contained fæcal matter.

For the sake of still further assurance that the sugar found in the liver was neither due to some accidental cause, nor immediately derived from food, we determined to deprive an animal of food for some days before examining the liver. The following experiment was accordingly performed:—

Exp. 6. A very large and powerful dog, in admirable condition, was subject to a rigid fast for seventy-two hours—three full days. Immediately after death, by section of the medulla oblongata, a portion of the liver was sliced off and immersed in ice and salt. Blood was then collected from the following sources:—

1st. From the portal vein.

2ndly. From the liver (*i. e.* blood which flowed from the liver when a portion of it was sliced off).

3rdly. From the right side of the heart.

4thly. From the aorta.

5thly. From the inferior vena cava.

Although these bloods were all treated in a similar manner, and tested with the same quantities of copper and soda, yet none of them gave unequivocal evidence of the presence of sugar, except that from the liver. The blood from the right side of the heart gave doubtful evidence. At first sight it may appear strange that the blood from the right side of the heart should contain scarcely an appreciable quantity of sugar, while that of the liver showed its presence very obviously; but this no doubt arose from the hepatic blood being in great part prevented from reaching the heart: 1st, on account of most of it escaping into the abdomen, when the portion of liver was cut off; and 2ndly, on account of its flow being in great measure arrested by the ligature of the portal vessels.

All the bloods, except the hepatic, seemed to be free of glucogen as well as sugar; for none of them, with that exception, gave any evidence of its presence after being treated with saliva in the usual way.

On examination of the frozen liver (after three hours), which, as

in the other cases, was not allowed to thaw before being put into boiling water, the decoction was found to reduce the copper readily.

On opening the stomach, nothing was found in it except some neutral mucus. The intestines were equally destitute of food, and in the rectum only a very small quantity of fæces was found; so there could be no doubt as to the animal being in a fasting condition.

The only point now remaining, was to determine quantitatively the increase in the amount of sugar in the liver after its removal from the body, and for that purpose we preferred operating on an animal fed on a mixed diet.

Exp. 7. A small dog, which had been previously fed on animal diet, received a full meal of bread and milk. Five hours afterwards the animal was pithed, and a portion of the liver rapidly sliced off and immersed in a freezing mixture. A ligature was placed on the portal vein, and its blood collected before the circulation had ceased.

On examination, this blood was found to contain a small quantity of sugar, derived no doubt from the food. Bernard, I believe, has erred in supposing that all the saccharine matter found in the animal organism is formed out of the glucogen produced in the liver. This, no doubt, is the case in the carnivora when the diet is restricted to food inconvertible into sugar in the alimentary canal, but cannot be regarded as the natural state of things either in the omnivora or herbivora; for the food of the latter not only contains sugar, but its amylaceous elements may be converted into that substance in the process of digestion. The sugar found in the bodies of animals fed on a mixed diet ought therefore to be regarded partly as the direct product of the food, and partly as derived from the glucogen formed in the liver.

Bernard's chief argument against this view is founded on the fact that the livers of dogs fed on a mixed diet contain no more sugar than those fed on purely animal food. In my opinion, however, this fact is not sufficient to decide the question; for, as the liver does not store up sugar, the quantity it at any time contains is no criterion of the amount produced in it. Moreover, the sugar derived from the food need not be expected to be found in the liver. Had Bernard gauged the sugar present in the blood, instead of that

in the liver, after each kind of diet, the result obtained would, I believe, have led him to a different conclusion. This being a point of great practical importance in the treatment of diabetes, I may be here permitted to mention that I have occasionally found nearly twice as much sugar in the blood of an animal on a mixed, than in that of one feeding on a purely flesh diet.

To return to the last experiment. About two hours after the death of the animal, portions of the frozen part of the liver, and of that which had been kept warm in the body of the animal, were carefully weighed, and the proportions of sugar they respectively contained estimated by volumetric analysis.

The portion of frozen liver was found to contain 0·333 per cent., and that of the other 1·55 per cent. of saccharine matter. It is thus seen that in two hours the sugar in the liver had augmented nearly fivefold. As Bernard has shown, the simple washing out of the liver by passing a stream of water through its vessels, would remove all the sugar anteriorly formed. On placing it again aside for a short time, a fresh portion of sugar would form in it at the expense of glucogen.

0·333 per cent. of sugar seems a small quantity; but if we suppose a liver weighing, as in man, not less than 50 oz., to contain 0·333 per cent., above 70 grs. of sugar would be present in it at the moment of death,—no very insignificant quantity, when it is recollected that sugar is removed from the liver with every pulsation of the heart, to be partly consumed, and that it is as continually supplied by the organ.

The results of the experiments now related do not therefore in any way countenance the notion that sugar is not produced in the healthy animal body. On the contrary, such conclusions as they afford are altogether in favour of the generally received views upon the subject.

From the preceding experiments the following conclusions may be drawn:—

1st. Sugar is a normal constituent of the blood of the general circulation.

2ndly. Portal blood of an animal on mixed diet contains sugar.

3rdly. Portal blood of a fasting animal, as well as of an animal fed solely on flesh, is devoid of sugar.

4thly. The livers of dogs contain sugar, whether the diet is animal or vegetable.

5thly. Under favourable circumstances, saccharine matter may be found in the liver of an animal after three entire days of rigid fasting.

6thly. The sugar found in the bodies of animals fed on mixed food is partly derived directly from the food, partly formed in the liver.

7thly. The livers of animals restricted to flesh diet possess the power of forming glucogen, which glucogen is at least in part transformed into sugar in the liver;—an inference which does not exclude the probability of glucogen (like starch in the vegetable organism) being transformed into other materials besides sugar.

8thly. As sugar is found in the liver at the moment of death, its presence cannot properly be ascribed to a *post mortem* change, but is to be regarded as the result of a natural condition.

II. "Hereditary Transmission of an Epileptiform Affection accidentally produced." By E. Brown-Séquard, M.D. Communicated by Dr. Sharpey, Sec. R.S. Received December 23, 1859.

It is well known that the number of facts which seem to prove that an accidentally produced affection may be transmitted by parents to their offspring is still small, and that serious objections have been raised against most, if not all, the facts of this kind. The following observations seem to show peremptorily that, at least in one species of animals, this kind of transmission may occur.

I have shown that certain injuries to the spinal cord, in Guinea-pigs and other Mammals, are followed, after a few weeks, by a convulsive disease, very much like epilepsy. For several years it has been frequently observed that the young of a number of those epileptic animals, which I kept in my laboratory, were at times attacked with epileptiform convulsions. For many months I have made regular observations on this curious subject, and I have ascertained, by careful watching, that six young guinea-pigs which had frequent attacks of convulsions, were the offspring of one male and two female